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UTILITY PATENT APPLICATION TRANSMITTAL

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Attorney Docket No. 3240 1

First Inventor or Application Identifier Warrington et al.

Title METHODS FOR IDENTIFYING AND USING MAINTENANCE GENES

Express Mail Label No. EL675506517US

APPLICATION ELEMENTS

See MPEP chapter 600 concerning design patent application contents.

1. ☒ Fee Transmittal Form (e.g., PTO/SB/17)
(Submit an original and a duplicate for fee processing)
2. ☐ Applicant claims small entity status.
See 37 CFR 1.27.
3. ☒ Specification [Total Pages 58]
(preferred arrangement set forth below)
 - Descriptive title of the Invention
 - Cross References to Related Applications
 - Statement Regarding Fed sponsored R & D
 - Background of the Invention
 - Brief Summary of the Invention
 - Brief Description of the Drawings (if filed)
 - Detailed Description
 - Claim(s)
 - Abstract of the Disclosure
4. ☐ Drawing(s) (35 U.S.C.113) [Total Sheets]
5. Oath or Declaration [Total Pages]
 - a. ☐ Newly executed (original or copy)
 - b. ☐ Copy from a prior application (37 CFR 1.63 (d))
(for a continuation/divisional with Box 17 completed)
 - i. ☐ **DELETION OF INVENTOR(S)**
Signed statement attached deleting inventor(s)
named in the prior application, see 37 CFR
1.63(d)(2) and 1.33(b).
6. ☐ Application Data Sheet. See 37 CFR 1.76

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7. ☐ CD-ROM or CD-R in duplicate, large table or
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8. Nucleotide and/or Amino Acid Sequence Submission
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 - a. ☐ Computer Readable Form (CRF)
 - b. Specification Sequence Listing on:
 - i. ☐ CD-ROM or CD-R (2 copies); or
 - ii. ☐ paper
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ACCOMPANYING APPLICATIONS PARTS

9. ☐ Assignment Papers (cover sheet & document(s))
10. ☐ 37 C.F.R. § 3.73(b) Statement ☐ Power of
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11. ☐ English Translation Document (if applicable)
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Telephone

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Name (Print/Type)

Wei Zhou

Registration No. (Attorney/Agent)

44,419

Signature

Date

October 19, 2000

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FEE TRANSMITTAL for FY 2001

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Application Number	
Filing Date	Oct. 19, 2000
First Named Inventor	Warrington et al
Examiner Name	
Group / Art Unit	
Attorney Docket No.	3240.1

TOTAL AMOUNT OF PAYMENT	(\$)	710
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- ☐ Applicant claims small entity status. See 37 CFR 1.27

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FEE CALCULATION

1. BASIC FILING FEE

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101	710	201	355	Utility filing fee	710
106	320	206	160	Design filing fee	
107	490	207	245	Plant filing fee	
108	710	208	355	Reissue filing fee	
114	150	214	75	Provisional filing fee	

SUBTOTAL (1)

(\$) 710

2. EXTRA CLAIM FEES

			Extra Claims		Fee from below		Fee Paid
Total Claims	12	-20**	= 0	X		=	0
Independent Claims	2	-3**	= 0	X		=	0
Multiple Dependent				X		=	0

Large Fee Code	Entity Fee (\$)	Small Fee Code	Entity Fee (\$)	Fee Description
103	18	203	9	Claims in excess of 20
102	80	202	40	Independent claims in excess of 3
104	270	204	135	Multiple dependent claim, if not paid
109	80	209	40	** Reissue independent claims over original patent
110	18	210	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2)	(\$)	0
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FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Fee Code	Entity Fee (\$)	Small Fee Code	Entity Fee (\$)	Fee Description	Fee Paid
105	130	205	65	Surcharge - late filing fee or oath	
127	50	227	25	Surcharge - late provisional filing fee or cover sheet.	
139	130	139	130	Non-English specification	
147	2,520	147	2,520	For filing a request for reexamination	
112	920*	112	920*	Requesting publication of SIR prior to Examiner action	
113	1,840*	113	1,840*	Requesting publication of SIR after Examiner action	
115	110	215	55	Extension for reply within first month	
116	390	216	195	Extension for reply within second month	
117	890	217	445	Extension for reply within third month	
118	1,390	218	695	Extension for reply within fourth month	
128	1,890	228	945	Extension for reply within fifth month	
119	310	219	155	Notice of Appeal	
120	310	220	155	Filing a brief in support of an appeal	
121	270	221	135	Request for oral hearing	
138	1,510	138	1,510	Petition to institute a public use proceeding	
140	110	240	55	Petition to revive – unavoidable	
141	1,240	241	620	Petition to revive – unintentional	
142	1,240	242	620	Utility issue fee (or reissue)	
143	440	243	220	Design issue fee	
144	600	244	300	Plant issue fee	
122	130	122	130	Petitions to the Commissioner	
123	50	123	50	Petitions related to provisional applications	
126	240	126	240	Submission of Information Disclosure Stmt	
581	40	581	40	Recording each patent assignment per property (times number of properties)	
146	710	246	355	Filing a submission after final rejection (37 CFR § 1.129(a))	
149	710	249	355	For each additional invention to be examined (37 CFR § 1.129(b))	
179	710	279	355	Request for Continued Examination (RCE)	
169	900	169	900	Request for expedited examination of a design application	

Other fee (specify)


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SUBTOTAL (3)

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SUBMITTED BY

Complete (if applicable)

<i>Name (Print/Type)</i>	Wei Zhou	<i>Registration No. Attorney/Agent</i>	44,419	<i>Telephone</i>	408-731-5699
<i>Signature</i>				<i>Date</i>	Oct. 19, 2000

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PATENT

Attorney Docket No. 3240.1

PATENT APPLICATION

METHODS FOR IDENTIFYING AND USING MAINTENANCE GENES

Inventor:

Janet A. Warrington, a citizen of the United States
residing at 1656 Christina Dr., Los Altos, CA 94024

Mamatha Mahadevappa, a citizen of India
residing at 1107 Derbyshire Dr., Cupertino, CA 95014

Archana Nair, a citizen of India
residing at 3589 Lochinvar Ave. #6
Santa Clara, CA 95051

Assignee:

Affymetrix, Inc.
a Corporation Organized under the laws of Delaware

Entity:

Large

Affymetrix, Inc.
Attn: Legal Department
3380 Central Expressway
Santa Clara, CA 95051
(408) 731-5000

METHODS FOR IDENTIFYING AND USING MAINTENANCE GENES

RELATED APPLICATIONS

This application claims the priority of U.S. Provisional Application Number 60/161,000, filed on October 21, 1999. The 60/161,000 application is incorporated

5 herein by reference in its entirety.

This application is related to U.S. Patent No. 6,033,860 which is incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

This application provides methods, compositions for identifying and using
10 maintenance genes. The methods and compositions have extensive practical applications in areas such as drug discovery and diagnostics.

Housekeeping genes, or maintenance genes, are those genes constitutively expressed to maintain cellular function (See, Watson, J.D., N.H. Hopkins, J.W. Roberts, J.A. Steitz, A.M. Weiner, A.M. *Molecular Biology of the Gene*, Vol.1, 1965).

15 Previously tens of genes have been reported as putative housekeeping genes. The genes previously reported were identified by conventional methods and the putative housekeeping role of the gene product is an incidental observation (Duhig, T., C. Ruhrberg, O. Mor, M. Fried. The Human Surfeit Locus. *Genomics*, **52**(1) 72-78, 1998; Hampsey, M. Molecular Genetics of the RNA Polymerase II General Transcriptional
20 Machinery. *Microbiol. Mol. Biol. Rev.* **62**(2):465-503, 1998; May, B.K., C.R. Bhasker, T.C. Cox.. Molecular Regulation of 5-Amniolevulinate Synthase Diseases Related to Heme Biosynthesis. *Mol. Biol. Med.*, **7**(5):405-421, 1990; Milner, C.M., R.D. Campbell.

Genes, Genes and More Genes in the Human Major Histocompatibility Complex.

Bioessays , **14**(8):565-571, 1992; Rifkind, R.A., P.A. Marks, A. Bank, M. Terada, G.M.

Maniatis, F.E. Reuben, E. Fibach. Erythroid Differentiation and the Cell Cycle: Some

Implications from Murine Foetal and Erythroleukemic Cells. *Ann.Immunol.***127**:887-893,

5 1976; Roberston, H.A. Immediate-Early Genes, Neuronal Plasticity, and Memory.

Biochem. *Cell Biol.*, **70**(9): 729-737, 1992; Russo-Marie, F. Macrophages and the

Glucocorticoids. *J Neuroimmunol*, **40**(2-3):281-286, 1992; Strehler, B.L., M.R. Freeman.

Randomness, Redundancy and Repair: Roles and Relevance to Biological Aging. *Mech.*

Aging Dev. **14**(1-2) 15-38, 1980; and Yamamoto, T., Y. Matsui, S. Natori, M. Obinata.

10 Cloning of a Housekeeping-Type Gene (MER5) Preferentially Expressed in Murine

Erythroleukemia Cells.*Gene* **80** 2:337-343, 1989).

Recently, massive parallel gene expression monitoring methods have been

developed to monitor the expression of a large number of genes using nucleic acid array

technology which was described in detail in, for example, U.S. Patent Numbers

15 5,871,928, 5,800,992 and 6,040,138; de Saizieu, *et al.*, 1998, Bacteria Transcript Imaging

by Hybridization of total RNA to Oligonucleotide Arrays, NATURE BIOTECHNOLOGY,

16:45-48; Wodicka *et al.*, 1997, Genome-wide Expression Monitoring in *Saccharomyces*

cerevisiae, NATURE BIOTECHNOLOGY 15:1359-1367; Lockhart *et al.*, 1996, Expression

Monitoring by Hybridization to High Density Oligonucleotide Arrays. NATURE

20 BIOTECHNOLOGY 14:1675-1680; Lander, 1999, Array of Hope, NATURE-GENETICS,

21(suppl.), at 3.

SUMMARY OF THE INVENTION

In one aspect of the current invention, methods for identifying a gene are provided. The methods include the steps of determining the expression of at least one hundred genes in at least two different types of tissues in two different developmental stages; and indicating a gene that is expressed at the same level in the tissues in the stages as the maintenance gene. In some embodiments, the method involves determining the expression of one thousand genes. In some preferred embodiments, the expression of candidate maintenance genes are measured in at least five different types of tissues. In one preferred embodiment, gene expression is determined using nucleic acid probe arrays such as high density oligonucleotide probe arrays, optical fiber arrays, spotted arrays (oligonucleotide, cDNA clones, cDNA fragments, etc.).

In preferred embodiments, a gene is considered as expressed at the same level if the variation of its expression is within 2, 5 or 10 fold. In another preferred embodiment, a gene is considered as expressed at the same level if the variation of its expression is not statistically significant.

In another aspect of the invention, methods are provided for comparing the expression of a gene in a plurality of biological samples. The methods include measuring the expression of at least three, five, seven or ten maintenance genes selected from the group of genes listed in table 1 or subset of the genes from table 1. The methods further include a step of evaluating the expression of the gene in the plurality of samples using the expression of the at least three, five or ten, maintenance genes. In some embodiments, the expression of a gene is adjusted using the expression of maintenance

genes as a control. For example, the expression measurement of a target gene may be divided by the expression measurements of maintenance genes.

Description of the Invention

Reference will now be made in detail to the preferred embodiments of the invention. While the invention will be described in conjunction with the preferred embodiments, it will be understood that they are not intended to limit the invention to these embodiments. On the contrary, the invention is intended to cover alternatives, modifications and equivalents, which may be included within the spirit and scope of the invention.

Methods for Gene Expression Monitoring:

Various techniques for large scale polymer synthesis and probe array manufacturing are known. Some examples include the U.S. Patents Nos.: 5,143,854, 5,242,979, 5,252,743, 5,324,663, 5,384,261, 5,405,783, 5,412,087, 5,424,186, 5,445,934, 5,451,683, 5,482,867, 5,489,678, 5,491,074, 5,510,270, 5,527,681, 5,550,215, 5,571,639, 5,593,839, 5,599,695, 5,624,711, 5,631,734, 5,677,195, 5,744,101, 5,744,305, 5,753,788, 5,770,456, 5,831,070, and 5,856,011, all of which are incorporated by reference in their entirety for all purposes.

The hybridization conditions between probe and target should be selected such that the specific recognition interaction, i.e., hybridization, of the two molecules, is both sufficiently specific and sufficiently stable. See, e.g., Hames and Higgins (1985) Nucleic Acid Hybridisation: A Practical Approach, IRL Press, Oxford. These conditions will be dependent both on the specific sequence and often on the guanine and cytosine (GC)

content of the complementary hybrid strands. The conditions may often be selected to be universally equally stable independent of the specific sequences involved. This typically will make use of a reagent such as an alkylammonium buffer. See, Wood et al. (1985)

"Base Composition-independent Hybridization in Tetramethylammonium Chloride: A

5 Method for Oligonucleotide Screening of Highly Complex Gene Libraries," Proc. Natl.

Acad. Sci. USA, 82:1585-1588; and Krupov et al. (1989) "An Oligonucleotide

Hybridization Approach to DNA Sequencing," FEBS Letters, 256:118-122; each of

which is hereby incorporated herein by reference. An alkylammonium buffer tends to

minimize differences in hybridization rate and stability due to GC content. By virtue of

10 the fact that sequences then hybridize with approximately equal affinity and stability,

there is relatively little bias in strength or kinetics of binding for particular sequences.

Temperature and salt conditions along with other buffer parameters should be selected

such that the kinetics of renaturation should be essentially independent of the specific

target subsequence or oligonucleotide probe involved. In order to ensure this, the

15 hybridization reactions will usually be performed in a single incubation of all the

substrate matrices together exposed to the identical same target probe solution under the

same conditions. The hybridization conditions will usually be selected to be sufficiently

specific such that the fidelity of base matching will be properly discriminated. Of course,

control hybridizations should be included to determine the stringency and kinetics of

20 hybridization. See for example, US Patent No. 5,871,928 which is hereby incorporated in

its entirety for all purposes. Another factor that can be adjusted to increase the ability of

targets to hybridize to probes, is the use of nucleic acid analogs or PNAs in the probes.

They can be built into the probes to create a more uniform set of hybridization conditions across the entire array. See U.S. Patent Application No. 08/630,427 which is hereby incorporated by reference in its entirety for all purposes.

Samples are then washed and stained using a robotic liquid handling machine such as the GeneChip® Fluidic Station 400 (Affymetrix, Inc., Santa Clara, CA). Fluidics stations have been described in, for example, US Patent Application Nos. 08/624,133 and 09/070,689. Finally, samples are placed on an automated loader which interfaces with a scanner such as the GeneArray™ scanner (Agilent Technologies). Scanners have been described in, for example, US Patent Nos. 5,578,832, 5,834,748, and 5,837,832, US Patent Application Nos. 08/456,598, 09/238,131, 08/856,642 (now allowed), 09/295,214, 08/456,782, 08/999,188, US Provisional Patent Application No. 60/106,397 and European Patent No. 97925605 each of which is hereby incorporated by reference in its entirety for all purposes.

The results are then analyzed using a computer program. Computer programs for the analysis of hybridization patterns on arrays have been described in, for example, U.S. Patent Nos. 5,733,729, and 5,795,716, U.S. Patent Application Nos. 09/309,328, 09/020,743, 08/531,137, 09/158,765, 08/584,754, 09/049,805, 08/828,952, 08/948,896 and U.S. Provisional Patent Application Nos. 60/033,053 and 60/085,118 each of which is incorporated by reference in its entirety for all purposes.

20 Methods for Detecting Maintenance Genes:

The term housekeeping gene was broadly defined as a gene that is constitutively expressed. In this application, housekeeping genes are also referred to as maintenance

genes. Generally, the housekeeping genes are critical to the processes that must be carried out for successful completion of the cell cycle and consequently play a key role in the activity and maintenance of every cell. It is likely that many genes may be constitutively expressed but in varying amounts in different tissues. These differences in level of abundance are probably more relevant to the characteristic function of each tissue than to the housekeeping/maintenance role.

Until recently the technical challenge of accurately measuring small differences in gene expression have been practically insurmountable, consequently there is little evidence to support the importance of small differences. One aspect of the invention provides methods, compositions, devices and algorithms for detecting Maintenance genes. The method comprises the step of measuring the expression of at least 50 genes, preferably 100 genes, more preferably more than 1000 genes, in a variety of tissues. The method further comprises the step of indicating that the gene is a Maintenance gene if the expression is the same in all the tissues of interest or in a subset of the tissues of interest. The term tissue, as used herein, is intended to describe a biological material from an organism. Therefore, an organ (or a homogenate of the organ), such the liver or kidney, may be referred to as a tissue. The methods are most suitable for simultaneously detecting a large number Maintenance genes. When it is used for simultaneous determination of a large number of Maintenance genes, the method includes the step of simultaneous monitoring of the expression of a large number of genes. Methods for monitoring a large number of genes are well known in the art and are described, for example, in the background section, *supra*. In some embodiments, the expression of a

gene in a number of tissue is measured. The gene is considered as expressed at the same level if it is expressed in all the tissues at levels within ten folds, preferably within fourfold and more preferably within two fold. In some embodiments, a gene is considered as expressed at the same level if it is expressed in all tissues with no

5 statistically difference. In the example that follows, genes were considered as expressed at the same level if they were expressed in all seven tissues at levels within fourfold. For most genes differences less than fourfold are probably not biologically significant but there is not enough data to conclude that a five or six-fold difference is more biologically significant than a three or four-fold difference (Cho, R.J., M.J. Campbell, E.A. Winzeler,
10 L. Steinmetz, A.Conway, L. Wodicka, T.G. Wolfsberg, A.E. Gabrielian, D. Landsman, D.J. Lockhart, R.W. Davis. A Genome-Wide Transcriptional Analysis of the Mitotic Cell Cycle. *Molecular Cell*, **2**: 65-73, 1998; Creanor, J., J.M. Mitchinson. Nucleoside Diphosphokinase, An Enzyme With Step Changes in Activity During the Cell Cycle of the Fission Yeast *Schizosaccharomyces Pombe*. *Journal of Cell Science* 207-215, 1986;
15 Klevecz, R.R.. *The Scientist* 22-24, 1999; Klevecz, R.R., S.A. Kaufman, R.M. Shymko, Cellular Clocks and Oscillators. *International Review of Cytology*, **86**:97-128, 1984). For a subset of genes it is likely that small differences have biological relevance such as the genes encoding proteins that function differently when bound to high affinity versus low affinity receptors or gene products triggering cellular cascades (Merchav, S.. The
20 Haematopoietic Effects of Growth Hormone and Insulin-Like Growth Factor-I. J. *Pediatr. Endocrin. Metab.* **11**(6):677-685, 1998; Skerry, T.M. Identification of Novel Signaling Pathways During Functional Adaptation of the Skeleton to Mechanical

Loading: The Role of Glutamate as a Paracrine Signaling Agent in the Skeleton. *J. Bone Miner Metab.* **17**(1): 66-70, 1999).

Maintenance Genes:

In another aspect of the invention, a subset of genes expressed at the same level in each of seven major tissues are identified as housekeeping genes (See, Table 1). Most of these genes have never before been specifically identified as belonging in this category. This information is useful for establishing average normal expression levels and will be useful as a reference in studies of normal expression variation (i.e.

www.HuGEindex.org). In one aspect of the invention, the maintenance genes described are used to establish average normal expression levels. In some embodiments, the expression of at least one of the genes listed in table 1, preferably at least two of the genes listed in table 1, more preferably at least 10 of the genes listed in table 1, and even more preferably at least 100 of the genes listed in table 1 is monitored along with the expression of a target gene (gene of interest). The change of the level of expression of the target gene will be evaluated using the expression of the maintenance gene(s) as a control.

Example Identification of Maintenance Genes

METHODS

Sample preparation

All samples were prepared from pools of human adult poly(A) RNA purchased from Clontech (Palo Alto, CA). The tissues screened are listed followed by the number of tissues pooled and the Clontech catalog number in parenthesis. Heart, 3 (6533-1), brain, 5

(6516-1), lung, 5 (6524-1), kidney, 8 (6538-1), pancreas, 10 (6539-1), uterus, 10 (6537-1), testis, 19 (6535-1). Poly(A) RNA was amplified and labeled with biotin following the procedure described by Wodicka et al., 1997⁽³²⁾. First strand cDNA synthesis was carried out at 37°C for 60 minutes. The amplified cRNA (target) was purified on an affinity resin (RNeasy, Qiagen) and quantitated.

Fragmentation, array hybridization and scanning

Labeled target was fragmented by incubation at 94°C for 35 minutes in the presence of 40 mM Tris-acetate pH 8.1, 100 mM potassium acetate, and 30 mM magnesium acetate. The hybridization solution consisted of 20 ug fragmented cRNA, 0.1 mg/ml sonicated herring sperm DNA in buffer containing 100mM MES, 1m[Na⁺], 20mMEDTA, 0.01%Tween 20 (MES). The hybridization mixture was heated to 99°C for 5 min. followed by incubation at 45°C for 5 min. before injection of the sample into the probe array cartridge. All hybridizations were performed in duplicate and were carried out at 45°C for 16 - 17 hr with mixing on a rotisserie at 60 rpm. Following hybridization, the solutions were removed, arrays were rinsed with 1X MES (100mM MES, 1m[Na⁺], 20mMEDTA, 0.01%Tween 20). Subsequent washing and staining of the arrays was carried out using the GeneChip® fluidics station protocol EukGE_WS2. The EukGE_WS2 protocol included two post hybridization washes, staining, and a post stain wash. The first wash consisted of 10 cycles of 2 mixes per cycle with Non Stringent Wash Buffer (6X SSPE, 0.01% Tween20, 0.005% Antifoam) at 25°C. The second wash consisted of 4 cycles of 15 mixes per cycle with Stringent Wash Buffer (100mm MES, 0.1M [Na⁺], 0.01% Tween

20) at 50°C. The probe arrays were stained for 10 minutes in streptavidin-phycoerythrin solution (SAPE) (1X MES solution, 0.005% antifoam, 10µg/ml SAPE (Molecular Probes, Eugene, OR) 2µg/µl acetylated BSA (Sigma, St. Louis, MO) at 25°C. The post stain wash consisted of 10 cycles of 4 mixes per cycle at 25°C. The probe arrays were
5 treated for 10 minutes in antibody solution (1X MES solution, 0.005% antifoam, 2µg/µl acetylated BSA, 0.1µg/µl normal goat IgG (Sigma Chemical, St. Louis MO), 3µg/µl antibody (goat), antistreptavidin, biotinylated (Vector Laboratories, Burlingame, CA) at 25°C. The final wash consisted of 15 cycles of 4 mixes per cycle at 30°C. Following washing and staining, probe arrays were scanned 2 times (multiple image scan) at 3 µm
10 resolution using the GeneChip® System confocal scanner made for Affymetrix Inc. by Hewlett Packard.

Probe arrays

The arrays were synthesized using light-directed combinatorial chemistry as described previously. The Hu6.8K_all GeneChip® probe arrays used for the current study contain
15 probe sets representing 7129 genes. The oligonucleotides are 25 bases in length. Probes are complementary and correspond to human genes registered in Unigene, GenBank and The Institute for Genomic Research Database (TIGR). Each probe set has oligonucleotides that are identical to sequence in the gene and oligonucleotides that contain a homomeric (base transversion) mismatch at the central base position of the
20 oligomer used for measuring cross hybridization. Probes are selected with a bias toward the 3' region of each gene. Probe pairs representing human genes such as GAPDH, B-actin, transferrin receptor and transcription factor ISGF-3 serve as internal controls for

monitoring RNA integrity. In addition, the probe arrays contain oligonucleotides representing sequences of bacterial genes, BioB, BioC, BioD, and one phage gene, Cre, as quantitative standards. Copy numbers are determined by correlating the known concentrations of the spiked standards with their hybridization. Copies per cell are
5 calculated based on the assumption that the average transcript length is 1 kb and there are 300,000 transcripts per cell.

Analysis

All samples were hybridized in duplicate and only those transcripts detected as present in duplicate hybridizations or absent in duplicate hybridizations are reported. Of the
10 transcripts present in duplicate hybridizations the hybridization values were within two fold. The values from the duplicate hybridizations were averaged. GeneChip® 3.0 software was used to scan and analyze the data. Microsoft Excel and Microsoft Access were also used for data analysis.

RESULT

15 Using GeneChip® probe arrays (Affymetrix, Santa Clara, CA), 695 genes that are expressed in common among heart, brain, lung, kidney, pancreas, uterus and testis were identified. 241 of the genes were detected at similar levels in each of the tissues; 44 genes were detected at low abundance, 72 detected at low-moderate abundance, 100 at moderate abundance, 13 at moderate-high abundance, and 12 at high abundance (See Table 1).

Table 1. Maintenance genes sorted by function. Abundance levels are binned by copies per cell where low, L, <5, low-moderate, LM >5<10, moderate, M, >10<50, moderate-high, MH, >50<100, high, H, >100.

Accession Number	Description	Abundance
ATPase		
M37104	mitochondrial ATPase coupling factor 6 subunit (ATP5A)	M
U51478	sodium/potassium-transporting ATPase beta-3 subunit	M
Z71460	vacuolar-type H(+)-ATPase 115 kDa subunit	LM
Channels, pores		
D31846	aquaporin-2 water channel	M
L08666	porin (por)	M
Cytochrome		
AC002115	COX6B (COXG) on chromosome 19 cosmids	M
M22760	nuclear-encoded mitochondrial cytochrome c oxidase Va subunit	M
L32977	ubiquinol cytochrome c reductase Rieske iron-sulphur protein	M
X13238	cytochrome c oxidase subunit VIc	M
X16560	COX VIIc subunit VIIc of cytochrome c oxidase	M
M28713	NADH-cytochrome b5 reductase (b5R)	LM

Dehydrogenase		
D90086	pyruvate dehydrogenase (EC 1.2.4.1) beta subunit	M
D43682	very-long-chain acyl-CoA dehydrogenase (VLCAD)	M
U17886	succinate dehydrogenase iron-protein subunit (sdhB)	LM
U05861	hepatic dihydrodiol dehydrogenase	L
L13761	dihydrolipoamide dehydrogenase	L
DNA binding		
J03827	Y box binding protein-1 (YB-1)	MH
M26730	mitochondrial ubiquinone-binding protein with an LTR-like sequence	M
X75593	rab 13	M
U79528	SR31747 binding protein 1	M
L37368	RNA-binding protein	M
U33821	tax 1-binding protein TXBP151	M
Z29505	nucleic acid binding protein sub2.3	M
U07857	18 kDa Alu RNA binding protein ,	M
M94556	mitochondrial specific single stranded DNA binding protein N31	LM
M28209	GTP-binding protein (RAB1)	LM
D13988	rab GDI	LM
U51334	putative RNA binding protein (RBP56) ,	LM

D43951	KIAA0099, (pumilio-like, putative DNA binding)	LM
U65928	Jun activation domain binding protein	L
Electron transfer		
X71129	electron transfer flavoprotein beta subunit	LM
J04058	electron transfer flavoprotein alpha-subunit	L
G protein related		
U20285	Gps1 (GPS1)	M
U45982	G protein-coupled receptor GPR-9-6	LM
U31384	G protein gamma-11 subunit	LM
X81625	Cl1 protein	L
HLA		
D32129	HLA class-I (HLA-A26) heavy chain	M
X03100	HLA-SB alpha (class II antigen)	M
X75091	HLA-DR associated protein II (PHAPII)	L
Heat shock		
J04988	90 kD heat shock protein	MH
L15189	mitochondrial HSP75	LM
Histone		
M11353	H3.3 histone class C	MH
U50079	histone deacetylase HD1	LM
X05855	histone H3.3	L

Interferons		
X57351	1-8D from interferon-inducible family	H
X59892	IFN-inducible gamma-2 protein	M
J00212	leukocyte interferon (ifn-alpha) alpha-f	L
Kinase		
M14676	src-like kinase (slk)	M
L08835	DM kinase (myotonic dystrophy kinase)	M
M30448	casein kinase II beta subunit	LM
Lysosome associated		
AJ000099	lysosomal hyaluronidase	M
U91932	AP-3 complex sigma3A subunit	M
M15182	beta-glucuronidase (lysosomal enzyme)	LM
M29877	alpha-L-fucosidase, (lysosomal enzyme)	LM
Membrane		
D29963	SFA-1, a member of transmembrane 4 superfamily	M
L10284	IP90, integral membrane protein, calnexin	M
U57877	nuclear-encoded mitochondrial integral membrane protein CII-3	LM
Metabolism		
D78361	ornithine decarboxylase antizyme	H
M33764	ornithine decarboxylase amino acid metabolism	M

HG2279-HT2375	Triosephosphate Isomerase	M
U86070	phosphomannomutase (carbohydrate metabolism)	LM
U32114	caveolin-2 (lipid metabolism)	L
Mitochondrial associated		
Z70759	mitochondrial 16S rRNA	H
M22538	nuclear-encoded mitochondrial NADH-ubiquinone reductase 24kD subunit	M
M22760	nuclear-encoded mitochondrial cytochrome c oxidase Va subunit	M
X60036	mitochondrial phosphate carrier protein	M
M37104	mitochondrial ATPase coupling factor 6 subunit (ATP5A)	M
M26730	mitochondrial ubiquinone-binding protein with an LTR-like sequence	M
X99728	NDUFV3, mitochondrial NADH ubiquinone oxidoreductase	M
U59309	nuclear-encoded mitochondrial fumarase precursor (FH)	LM
L15189	mitochondrial HSP75	LM
M94556	mitochondrial specific single stranded DNA binding protein	LM
U57877	nuclear-encoded mitochondrial integral membrane protein CII-3	LM

L07033	hydroxymethylglutaryl-CoA lyase	LM
U15174	Nip3 (NIP3) (mitochondrial, pro-apoptotic protein family)	L
Phosphatase		
U45975	phosphatidylinositol (4,5) biphosphate 5-phosphatase homolog	M
X74008	phosphatase 1 gamma	LM
X81003	HCG V (phosphatase inhibitor)	LM
M65254	phosphatase 2A 65 kDa regulatory subunit-beta	L
Polymerase		
Z27113	RNA polymerase II subunit 14.4 kD	M
U37690	RNA polymerase II subunit (hsRBP10)	M
Z47727	RNA polymerase II subunit	LM
Protease, proteinase related		
L02426	26S protease (S4) regulatory subunit	M
M23254	Ca2-activated neutral protease large subunit (CANP)	M
X12451	pro-cathepsin L (major excreted protein MEP)	M
S69272	cytoplasmic antiproteinase, 38kD intracellular serine proteinase inhibitor	M
Proteasome		
D29012	proteasome subunit Y	M
D26598	proteasome subunit HsC10-II	M

D26599	proteasome subunit HsC7-I	M
D38047	26S proteasome subunit p31	M
AB003177	proteasome subunit p27	LM
D00763	proteasome subunit HC9	LM
D50063	proteasome subunit p40_ / Mov34 protein,	LM
X61970	macropain subunit zeta (proteasome)	LM
X95586	MB1	LM
D00760	proteasome subunit HC3	L
D00762	proteasome subunit HC8	L
Receptor and receptor associated proteins		
M63959	alpha-2-macroglobulin receptor-associated protein	M
D23673	insulin receptor substrate-1-like (IRS-1)	M
X07979	fibronectin receptor beta subunit	M
U83239	CC chemokine STCP-1 (immune function, T-receptor assoc)	M
M88279	immunophilin (FKBP52)	M
U45982	G protein-coupled receptor GPR-9-6	LM
X56253	MPR46 46kd mannose 6-phosphate receptor	LM
X80763	5-HT2c receptor	LM
L40357	thyroid receptor interactor (TRIP7)	L
Reductase		

M22538	nuclear-encoded mitochondrial NADH-ubiquinone reductase 24kD subunit	M
X91247	thioredoxin reductase	LM
X15414	aldose reductase (EC 1.1.1.2)	LM
M28713	NADH-cytochrome b5 reductase (b5R)	LM
Repair		
U07418	DNA mismatch repair (hmlh1)	L
U49785	D-dopachrome tautomerase	LM
Replication		
J05249	replication protein A 32-kD subunit	LM
Ribonucleoprotein		
HG3076-HT3238	heterogeneous nuclear ribonucleoprotein K, alt.splice 1	M
X16135	novel heterogeneous nuclear RNP protein, L protein	M
X78136	hnRNP-E2	M
M94630	hnRNP-C like protein	M
M16342	nuclear ribonucleoprotein particle (hnRNP) C protein	LM
Z23064	hnRNP G protein	L
Ribosomal		
X81625	ribosomal protein L37a (RPL37A)	H
Z12962	homologue to yeast ribosomal protein L41	H
HG3214-HT3391	Metallopanstimulin , MPS-1 (S27, Zinc finger)	H

HG1800-HT1823	ribosomal protein S20	H
U14973	ribosomal protein S29	H
Z26876	ribosomal protein L38	MH
M77232	ribosomal protein S6	MH
HG821-HT821	ribosomal protein S13	MH
M13934	RPS14, ribosomal protein S14	MH
Ribosylation		
M84332	ADP-ribosylation factor 1	M
M36341	ADP-ribosylation factor 4 (ARF4)	LM
Signal transduction		
D49396	Apo1 (MER5-like protein)	L
Structure		
U57341	neurofilament triplet L protein	MH
Z19554	vimentin	MH
X51521	ezrin	M
HG2238-HT2321	nuclear mitotic apparatus protein 1, alt.splice form 2	M
M64571	microtubule-associated protein 4	M
M31013	nonmuscle myosin heavy chain (NMHC)	M
V00599	fragment encoding beta-tubulin (D-beta-1)	M
U24105	coatamer protein (HEPCOP) ,	M
M95627	angio-associated migratory cell protein (AAMP)	LM

D38549	KIAA0068	LM
U56637	capping protein alpha subunit isoform 1	LM
X72964	caltractin	LM
X70476	subunit of coatomer complex	LM
D28915	hepatitis C-associated microtubular aggregate protein p44	L
X82103	beta-COP	L
Synthases and synthetases		
D14710	ATP synthase alpha subunit	MH
X76013	QRSHs, glutaminyl-tRNA synthetase	M
X83218	ATP synthase	M
X60221	H ⁺ -ATP synthase subunit b	M
D31890	KIAA0070	M
U09510	glycyl-tRNA synthetase	LM
U79262	deoxyhypusine synthase	LM
J03473	poly(ADP-ribose) synthetase	LM
X94754	yeast methionyl-tRNA synthetase homologue	LM
Transcription		
L49380	transcription factor ZFM1	M
U95040	transcriptional corepressor hKAP1/TIF1B	M
U10323	nuclear factor NF45	M
L12168	adenylyl cyclase-associated protein (CAP) ,	M

M97935	transcription factor ISGF-3 sequence	LM
X52882	t-complex polypeptide 1	LM
L19067	NF-kappa-B transcription factor p65 subunit	L
D63478	KIAA0144	L
U15782	cleavage stimulation factor 77kDa subunit (polyadenylation)	L
L20298	transcription factor (CBFB)	L
Transferase		
U56417	lysophosphatidic acid acyltransferase-alpha	M
U62739	branched-chain amino acid aminotransferase (ECA40)	M
Y08200	rab geranylgeranyl transferase, alpha-subunit	M
U82010	heme A: farnesyltransferase (COX10)	LM
U86529	glutathione transferase Zeta 1 (GSTZ1)	LM
D26535	dihydrolipoamide succinyltransferase	L
Transformation related		
U50523	BRCA2 region	M
U57342	myelodysplasia/myeloid leukemia factor 2 (MLF2) ,	M
HG4541-HT4946	transformation-related protein	M
M15990	c-yes-1	L
L12535	RSU-1/RSP-1 (Ras suppressor)	L
Translation, initiation and elongation		

J04617	elongation factor EF-1-alpha	H
X51466	elongation factor 2	MH
L26247	sui1,N278 iso1	MH
U46025	translation initiation factor eIF-3 p110 subunit	M
X55733	initiation factor 4B	LM
X98743	RNA helicase (Myc-regulated dead box protein)	L
Transport		
U36341	SLC6A8 (creatine transporter)	M
U51478	sodium/potassium-transporting ATPase beta-3 subunit	M
X81817	BAP31 (ER, protein sorting)	M
Y00281	ribophorin I (ER)	M
Y00282	ribophorin II (ER)	M
U70660	copper transport protein HAH1	LM
U41740	trans-Golgi p230	LM
X12791	signal recognition particle,SRP 19kD protein (ER)	L
Ubiquitin related		
X56997	UbA52 coding for ubiquitin-52 amino acid fusion protein	MH
M26880	ubiquitin	M
U46751	phosphotyrosine independent ligand p62 for the Lck SH2 domain	M
U39317	E2 ubiquitin conjugating enzyme UbcH5B (UBCH5B) ,	L

Zinc finger		
HG3214-HT3391	Metallopanstimulin , MPS-1 (S27, Zinc finger)	H
X70394	OZF	L
U09412	zinc finger protein ZNF134	L
HG3454-HT3647	zinc finger protein 20	L
Undefined		
X67698	unknown product	M
L11066	unknown product	M
U79294	unknown product	M
D28124	unknown product	M
D21261	KIAA0120	M
D87451	KIAA0262	M
D14694	KIAA0024	M
ISGF3A/M97935	unknown product	LM
L20773	unknown product	LM
D42043	KIAA0084	LM
D50911	KIAA0121	LM
D79994	KIAA0172	LM
D29643	KIAA0115	LM
D14662	KIAA0106	LM
D86963	KIAA0208	LM

D21853	KIAA0111	LM
D63476	KIAA0142	LM
D42087	KIAA0118	L
D30756	KIAA0049	L
D80004	KIAA0182	L
D79993	KIAA0171	L
L40395	unknown product	L
Others		
X98482	TNNT2, (troponin)	H
U06155	chromosome 1q subtelomeric sequence	H
M33680	26-kDa cell surface protein TAPA-1	H
M13450	esterase D	M
U11861	G10 homolog, edg-2	M
U62317	hypothetical protein 384D8_2 on chromosome 22q13 (other)	M
HG3991-HT4261	Cpg-enriched DNA (other)	M
X80199	MLN51	M
X80200	MLN62	M
U46570	tetratricopeptide repeat protein (tpr1) N297 (other)	M
HG3597-HT3800	major histocompatibility complex, class I	M
X71428	fus (nuclear RNA binding protein)	M

U73824	p97	M
Y00433	glutathione peroxidase (peroxide clearance)	M
U02493	54 kDa protein	M
U88964	HEM45	LM
D78129	squalene epoxidase (sterol biosynthesis)	LM
D43951	KIAA0099, (pumilio-like, putative DNA binding)	LM
X96484	DGCR6 protein (organization, migration during development)	LM
HG1155-HT4822	colony-stimulating factor 1, macrophage, alt. splice 3	LM
L38932	GT197 N305	LM
X66397	tpr	LM
L42572	p87/89 (ER transmembrane protein)	LM
X80695	OXA1Hs (cytochrome oxidase assembly)	LM
Y00097	p68 (membrane associated, calcium binding protein)	LM
Z48042	GPI-anchored protein p137	LM
Z35093	SURF-1 (Surfeit gene family, biogenesis of cytochrome C oxidase)	LM
U54644	tub homolog	LM
Z93784	mouse brain protein E46-like sequence	L
L38616	brain and reproductive organ-expressed protein (BRE)	L
D63506	unc-18 homologue	L

U18009	human gene on chromosome 17q21	L
L27476	X104 (membrane associated, kinase containing protein family)	L
M73720	mast cell carboxypeptidase A (MC-CPA)	L

For example, no difference in expression level was detected for 5 of the genes and a two-fold difference was detected for 46 of the genes. 454 genes are expressed in all seven tissues but vary in expression level by more than fourfold. 333 of the genes vary in expression level by 5-10 fold. Included in this subset are genes frequently used as controls in standard expression analysis including beta actin (M10277) varying by 7-fold with highest expression in brain and uterus and lowest expression in heart, and GAPDH (M33197) varying by 8-fold with highest expression in brain, heart and kidney and lowest in pancreas. Another form of beta actin (X00351) varied by 22-fold with highest expression in uterus and lowest in pancreas. Alpha actin (X13839) varied by 23-fold and gamma actin (M19283) by 9-fold. 40 genes expressed in all seven tissues differ in transcript levels by greater than 19 fold and of these eight differ by more than 50-fold, including COX7A muscle isoform (M83186) varying by 52-fold, highest in heart, lowest in kidney, pancreas and testis, lectin (J04456) varying by 58-fold, highest in uterus, lowest in kidney and pancreas, myosin heavy chain (AF001548) varying by 61-fold, highest in uterus, lowest in brain and pancreas, elongation factor-1 delta (Z21507) varying by 69-fold, highest in pancreas, lowest in lung and kidney, RNA polymerase II elongation protein (Z47087) varying by 70-fold, highest in brain, lowest in pancreas,

extracellular mRNA for glutathione peroxidase (D00632) varying by 78-fold, highest in kidney, lowest in brain, pancreas and testis, 14-9-9 protein eta chain (D78577) varying by 81-fold, highest in brain, lowest in testis, and L-arginine:glycine amidinotransferase (S68805) varying by 133-fold, highest in pancreas and lowest in heart and lung.

5 In the same experiments, genes expressed uniquely in each of the seven tissues were also identified (Table II). For instance, in heart there were 4 transcripts not detected in the other 6 tissues; muscle glycogen synthase (J04501), NADH oxidoreductase subunit (L04490), MLC-1 V/Sb isoform (M24248) and cytokine inducible nuclear protein (X83703). Twenty nine uniquely expressed transcripts were identified in the kidney including many that are expected such as potassium channel ROM-K3 (U65406) and renal Na/Pi cotransporter (L13258) as well as genes of unknown function such as a gene that maps to chromosome 19 (U95090). 45 uniquely expressed transcripts were detected in uterus, 28 in pancreas and 19 in lung. Not surprisingly, the greatest number of uniquely expressed genes, 91 and 94 respectively, were found in brain and testis.

Table II. Genes Uniquely Expressed in a Comparison of Eleven Human Tissues

Accession No.	Description	Bin*
Uniquely Expressed in Adult Heart		
J04501	Muscle glycogen synthase	M
M24248	MLC-1 V/Sb isoform	M
X83703	Cytokine inducible nuclear protein	LM
Uniquely Expressed in Fetal Kidney		
D88532	P55pik	L
M26901	Renin	M
M81829	Somatostatin receptor isoform 1	L
U19107	ZNF127	L
U19906	Arginine vasopressin receptor 1 (AVPR1)	L
U34301	Nonmuscle myosin heavy chain IIB	LM
X58431	HOX 2.2	M

Z67743	CLC-7 chloride channel protein	LM
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Uniquely Expressed in Fetal Liver

AF000573	Homogentisate 1,2-dioxygenase	LM
D00097	Amyloid P component (SAP)	M
D16611	Coproporphyrinogen oxidase	M
D16626	Histidase	M
D21063	KIAA0030	M
D26361	KIAA0042	L
D38535	PK-120	H
D38537	Protoporphyrinogen oxidase	M
D42055	KIAA0093	L
D49357	S-adenosylmethionine synthetase	LM
D49742	HGF activator like protein	M
D79988	KIAA0166	L
D84454	UDP-galactose translocator	LM
D87116	MAP kinase kinase 3b	M
D90282	Carbamyl phosphate synthetase I (EC 6.3.4.16)	MH
HG1148-HT1148	Lipopolysaccharide-Binding Protein	H
HG1227-HT1227	Collagen, Type II, Alpha 1	M
HG1649-HT1652	Elastase 1	M
HG2730-HT2827	Fibrinogen, A Alpha Polypeptide, Alt. Splice 2, E	H
HG3105-HT3281	ATPase, Cu ²⁺ Transporting	L
HG3565-HT3768	Zinc Finger Protein	M
HG627-HT5097	Rhesus (Rh) Blood Group System Ce-Antigen, Alt. Splice 2, Rhvi	MH
J00116	Collagen COL2A1	M
J02982	Glycophorin B	MH
J03474	Serum amyloid A	H
J03626	UMPS	L
J05070	Type IV collagenase	L
J05500	Beta-spectrin (SPTB)	M
K01383	Metallothionein-I-A	MH
K02402	Coagulation factor IX	M
L00190	Antithrombin III (ATAIII)	H
L01664	Eosinophil Charcot-Leyden crystal (CLC) protein (lysophospholipase)	L
L06133	Putative Cu ⁺⁺ -transporting P-type ATPase	L
L09708	Complement component 2 (C2), allele b	MH
L11244	C4b-binding protein beta-chain	M
L31860	Glycophorin A, MN-types (GYPA)	M
L32140	Afamin	M
L34081	Bile acid CoA: Amino acid N-acyltransferase	LM

L48516	Paraoxonase 3 (PON3)	M
L76571	Nuclear hormone receptor (shp)	M
L77567	Mitochondrial citrate transport protein (CTP)	M
M10014	Fibrinogen gamma chain and gamma-prime chain	H
M10058	Asialoglycoprotein receptor H1	M
M10950	Alpha-fetoprotein (AFP)	M
M11025	Asialoglycoprotein receptor H2	M
M11567	Angiogenin and three Alu repetitive sequences	M
M13699	Ceruloplasmin (ferroxidase)	MH
M14091	Thyroxine-binding globulin	M
M15205	Thymidine kinase with clustered Alu repeats in the introns	M
M16961	Alpha-2-HS-glycoprotein alpha and beta chain	H
M16967	Coagulation factor V	M
M16973	Complement protein C8 beta subunit	M
M17262	Prothrombin (F2) gene, and Alu and KpnI repeats	H
M19481	Follistatin	LM
M19828	Apolipoprotein B-100 (apoB)	H
M20786	Alpha-2-plasmin inhibitor	MH
M22638	LYL-1 protein	M
M22898	Phosphoprotein p53	L
M27819	Anion exchange protein 1 (AE1, band 3)	MH
M29194	Triglyceride lipase	M
M36803	Hemopexin	H
M58569	Fibrinogen alpha-subunit bipartite transcript of extended (alpha-E) variant	H
M58600	Heparin cofactor II (HCF2), exons 1 through 5	H
M59820	Granulocyte colony-stimulating factor receptor (CSF3R)	LM
M60298	Erythrocyte membrane protein band 4.2 (EPB42)	MH
M61827	Leukosialin (CD43)	LM
M61855	Cytochrome P4502C9 (CYP2C9), clone 25	L
M64554	F13A1 gene (coagulation factor XIIIb)	M
M68895	Alcohol dehydrogenase 6	L
M71243	Glycophorin Sta (type A) exons 3 and 4	MH
M75106	Prepro-plasma carboxypeptidase B	MH
M86873	Type A plasminogen related	M
S42457	Photoreceptor cGMP-gated channel	L
S48983	SAA4, serum amyloid A	M
S70004	Glycogen synthase	LM
S72370	Pyruvate carboxylase	LM
S77393	Transcript ch138	LM
S77763	Nuclear factor erythroid 2	M

S77893	Glycophorin SAT	MH
S78234	Nuc2 homolog	LM
U00001	Homologue of <i>S. pombe</i> nuc2+ and <i>A. nidulans</i> bima	L
U01317	Epsilon-globin	LM
U05255	Glycophorin HeP2	H
U08006	Complement 8 alpha subunit (C8A)	M
U12778	Acyl-CoA dehydrogenase	LM
U13061	Dehydroepiandrosterone sulfotransferase (STD)	L
U14518	Centromere protein-A (CENP-A)	L
U18919	Clone pOV-2	L
U20530	Bone phosphoprotein spp-24 precursor	M
U20979	Chromatin assembly factor-I p150 subunit	L
U32989	Tryptophan oxygenase (TDO)	M
U61836	Putative cyclin G1 interacting protein	M
U65404	Erythroid-specific transcription factor EKLF	M
U72515	C3f	M
U73167	H_LUCA14.2a	M
U73524	Putative ATP/GTP-binding protein (HEAB)	L
U90544	Sodium phosphate transporter (NPT3)	M
V01514	Alpha-fetoprotein (AFP)	H
X02176	Complement component C9	M
X02544	Alpha1-acid glycoprotein (orosomucoid)	H
X03473	Histone H1(0)	M
X04898	Apolipoprotein	H
X05309	C3b/C4b receptor (CR1) F allotype	L
X06482	Theta 1-globin	M
X06562	Growth hormone receptor	L
X13293	B-myb	M
X13589	Aromatase (estrogen synthetase)	LM
X14329	Carboxypeptidase N small subunit (EC 3.4.17.3)	LM
X14690	Plasma inter-alpha-trypsin inhibitor heavy chain H(3)	H
X15422	Mannose-binding protein C	M
X16260	Inter-alpha-trypsin inhibitor subunit 3	H
X16983	Integrin alpha-4 subunit	L
X17059	NAT1 gene for arylamine N-acetyltransferase	L
X17254	Transcription factor Eryf1	M
X51688	Cyclin A	LM
X53414	Peroxisomal L-alanine:glyoxylate aminotransferase	MH
X55668	Proteinase 3	M
X56692	C-reactive protein	M
X56741	Rab8	L

X58199	Beta adducin	M
X59618	RR2 small subunit ribonucleotide reductase	LM
X59711	CAAT-box DNA binding protein subunit A	L
X59812	CYP 27 vitamin D3 25-hydroxylase	M
X62822	Beta-galactoside alpha-2,6-sialyltransferase	LM
X63097	Rhesus polypeptide (RhXIII)	L
X64594	Erythrocyte plasma membrane glycoprotein	MH
X64877	Serum protein	LM
X65550	Antigen of monoclonal antibody Ki-67	L
X74330	DNA primase (subunit p48)	L
X75315	Seb4B	M
X77737	Red cell anion exchanger (EPB3, AE1, Band 3)	H
X80907	P85 beta subunit of phosphatidyl-inositol-3-kinase	M
X91148	Microsomal triglyceride transfer protein	LM
X98337	Complement factor H-related protein 4	M
Y00317	Liver microsomal UDP-glucuronosyltransferase (UDPGT)	LM
Z15005	CENP-E	LM
Z26248	Eosinophil granule major basic protein	LM
Z28339	Delta 4-3-oxosteroid 5 beta-reductase	LM
Z32684	XK membrane transport protein	M
Z83821	DNA sequence from PAC 296K21 on chromosome X contains cytokeratin exon, delta-aminolevulinate synthase (erythroid); 5- aminolevulinic acid synthase	H
Z84721	DNA sequence from cosmid GG1 from a contig from the tip of the short arm of chromosome 16, spanning 2Mb of 16p13.3	H

Uniquely Expressed in Fetal Lung

D87071	KIAA0233	LM
HG4638-HT5050	Spliceosomal Protein Sap 49	L
U18671	Stat2	L
U40434	Mesothelin or CAK1 antigen precursor	LM
X52896	Dermal fibroblast elastin	M
X97748	PTX3	LM

Uniquely Expressed in Adult Brain

D87463	KIAA0273	M
HG2259-HT2348	Tubulin, Alpha 1, Isoform 44	M
HG3437-HT3628	Myelin Proteolipid Protein, Alt. Splice 2	H
L00354	Cholecystokinin (CCK)	M
L76224	NMDA receptor	M
L76627	Metabotropic glutamate receptor 1 alpha (mGluR1alpha)	L

M55267	EV12 protein	LM
M59488	S100 protein beta-subunit	M
S50017	2',3'-cyclic nucleotide 3'-phosphodiesterase	M
S69965	Beta-synuclein	M
U01824	Glutamate/aspartate transporter II	M
U06698	Neuronal kinesin heavy chain	LM
U27768	RGP4	M
U62801	Protease M	M
U82532	GDI-dissociation inhibitor RhoGDIgamma	LM
X59065	FGF, exon 3	M
X64810	PC1/PC3	LM
X73882	E-MAP-115	LM
X99076	NRGN, exons 2, 3 & 4 (joined CDS)	H
Z48051	Myelin oligodendrocyte glycoprotein (MOG)	M

Uniquely Expressed in Adult Kidney

J04093	Phenol UDP-glucuronosyltransferase (UDPGT)	LM
L13258	Renal Na/Pi-cotransporter	M
M19878	Calbindin 27, exons 1 and 2, and Alu repeat	M
S77576	ERV9 reverse transcriptase homolog (clone RT18)	L
U17418	Hormone/parathyroid hormone-related peptide receptor	M
X13227	D-amino acid oxidase	M
X60708	PcHDP7, liver dipeptidyl peptidase IV	L

Uniquely Expressed in Adult Uterus

D21337	Collagen	L
D86961	KIAA0206	L
HG721-HT4828	Placental Protein 14, Endometrial Alpha 2 Globulin, Alt. Splice 3	M
L00205	K6b (epidermal keratin, type II)	L
L02785	Colon mucosa-associated (DRA)	L
L06419	Lysyl hydroxylase (PLOD)	LM
L08044	Intestinal trefoil factor	LM
L10343	Elafin	M
L14848	MHC class I-related protein	L
M19888	Small proline rich protein (sprI)	M
M21121	T cell-specific protein (RANTES)	L
M21389	Keratin type II (58 kD)	M
M55543	Guanylate binding protein isoform II (GBP-2)	L
M59979	Prostaglandin endoperoxide synthase	L
M60284	Neurokinin A receptor (NK-2R)	LM
M62783	Alpha-N-acetylgalactosaminidase	L

M85276	NKG5	M
M86757	Psoriasin	M
M86849	Connexin 26 (GJB2)	L
M96233	Transferase class mu number 4 (GSTM4)	LM
S66896	Squamous cell carcinoma antigen, serine protease inhibitor	L
S72493	Keratin 16 homolog	M
S81661	Keratinocyte growth factor	L
U07969	Intestinal peptide-associated transporter HPT-1	L
U09278	Fibroblast activation protein	L
U09584	PL6 protein (PL6)	L
U11717	Calcium activated potassium channel (hslo)	L
U24488	Tenascin-X (XA)	M
U25138	MaxiK potassium channel beta subunit	M
U37283	Microfibril-associated glycoprotein-2 MAGP-2	M
U43185	Signal transducer and activator of transcription Stat5A	L
U60325	DNA polymerase gamma, nuclear gene encoding mitochondrial protein	L
U76764	CD97	LM
U81523	Endometrial bleeding associated factor	M
X03635	Oestrogen receptor	M
X06256	Fibronectin receptor alpha subunit	LM
X07695	Cytokeratin 4 C-terminal region	M
X07696	Cytokeratin 15	L
X16662	Vascular anticoagulant-beta (VAC-beta)	L
X54162	64 Kd autoantigen expressed in thyroid and extra-ocular muscle	M
X63629	P cadherin	L
X75535	PxF protein	L
X83857	Prostaglandin E receptor (EP3a1)	L
X92521	MMP-19 protein	L
X93510	37 kDa LIM domain protein	LM
X96719	AICL (activation-induced C-type lectin)	LM
X98311	Carcinoembryonic antigen, CGM2	L
Y07755	S100A2, exon 1, 2 and 3	M

Uniquely Expressed in Adult Testis

D17570	Zona-pellucida-binding protein (sp38).	M
D50925	KIAA0135	L
D64109	Tob family	L
D78333	Testis-specific TCP20	M
D78334	Ankyrin motif	MH
HG2075-HT2137	Camp-Responsive Element Modulator, Alt. Splice 1	M
HG36-HT4101	Polymyositis/Scleroderma (Pm-Scl) Autoantigen, Alt. Splice 2	L

HG3725-HT3981	Insulin-Like Leydig Hormone	M
HG4316-HT4586	Transketolase-Like Protein	L
L01042	HIV1 tata element modulatory factor	L
L07515	Heterochromatin protein homologue (HP1)	LM
L14754	DNA-binding protein (SMBP2)	LM
L22214	Denosine A1 receptor (ADORA1), exons 1-6	L
L36861	Guanylate cyclase activating protein (GCAP), exons 1-4	L
L42324	G protein-linked receptor (GPCR)	L
L76687	Grb14	L
M13981	Inhibin A-subunit	M
M14565	Cholesterol side-chain cleavage enzyme P450scc	L
M21539	Small proline rich protein (sprII)	L
M31606	Phosphorylase kinase (PSK-C3)	M
M63256	Major Yo paraneoplastic antigen (CDR2)	L
M73077	Glucocorticoid receptor repression factor 1 (GRF-1)	LM
M86808	Pyruvate dehydrogenase complex (PDHA2)	L
M91438	Kazal-type serine proteinase (HUSI-II)	M
S68134	CREM, cyclic AMP-responsive element modulator beta isoform	LM
S78873	Zn2+ binding protein/guanine nucleotide exchange factor	L
U03644	Recepin	L
U10362	GP36b glycoprotein	L
U13680	Lactate dehydrogenase-C (LDH-C)	M
U15422	Protamine 1 (PRM1), protamine 2 (PRM2) and transition protein 2 (TNP2)	H
U17032	P190-B (p190-B)	L
U17280	Steroidogenic acute regulatory protein (StAR)	LM
U19147	GAGE-6 protein	LM
U20362	Tg737	LM
U22815	LAR-interacting protein 1a	L
U31929	Orphan nuclear receptor (DAX1)	L
U38175	HuR RNA binding protein (HuR)	L
U41763	Muscle specific clathrin heavy chain (CLTD)	L
U43944	Breast cancer cytosolic NADP(+)-dependent malic enzyme	L
U47054	Putative mono-ADP-ribosyltransferase (htMART)	LM
U58970	Putative outer mitochondrial membrane 34 kDa Translocase hTOM34	M
U60665	Testis specific basic protein (TSBP)	L
U65011	Preferentially expressed antigen of melanoma (PRAME)	LM
U65092	Melanocyte-specific gene 1 (msg1)	M
U65533	Regulator of nonsense transcript stability (RENT1)	L
U65918	Putative RNA binding protein (DAZH)	L
U66726	Testis specific RNA binding protein (SPGYLA)	LM

U70981	Interleukin-13 receptor	L
U78722	Zinc finger protein 165 (Zpf165)	L
U79266	Clone 23627	L
U84720	Export protein Rae1 (RAE1)	LM
U89606	Pyridoxal kinase	M
X04445	InhA gene exon 1 (and joined CDS)	LM
X05246	Testis-specific PGK-2 gene for phosphoglycerate kinase (ATP:3-phospho-D-glycerate 1-phosphotransferase, EC 2.7.2.3)	M
X07948	Transition protein 1 (TP1)	H
X12433	PHS1-2, ORF homologous to membrane Receptor proteins	LM
X14968	RII-alpha subunit of cAMP dependent protein kinase	L
X68285	Glycerol kinase	L
X69398	OA3 antigenic surface determinant	L
X70218	Protein phosphatase X	LM
X78706	Carnitine acetyltransferase	M
X78711	Glycerol kinase testis specific 1	L
X78712	Glycerol kinase testis specific 2	M
X79200	SYT-SSX, synovial sarcoma translocation junction	M
X89960	Mitochondrial capsule selenoprotein	M
X95239	Cysteine-rich secretory protein-2/type I	M
X99374	Fertilin beta	L
Y00970	Acrosin (EC 3.4.21.10)	M
Y12856	AMP-activated protein kinase alpha-1	L
Z22780	Cylicin	L
Z46788	Cylicin II	L
Z46967	Calicin	M
Z48570	Sp17	LM
Z49105	HD21	M
Z50115	Thimet oligopeptidase (metalloproteinase)	L
Z75190	Apolipoprotein E receptor 2.	L

Uniquely Expressed in Fetal Brain

HG1996-HT2044	Guanine Nucleotide-Binding Protein Rap2, Ras-Oncogene Related	LM
HG4063-HT4333	Transcription Factor Hbf-2	M
L07919	Homeodomain protein DLX-2	M
L13744	AF-9	LM
M64358	Rhom-3	LM
M88461	Neuropeptide Y peptide YY receptor	M
U00802	Drebrin E2 (DBN1)	M
U04735	Microsomal stress 70 protein ATPase core (stch)	L
U09413	Zinc finger protein ZNF135	L

U11701	LIM-homeobox domain protein (hLH-2)	M
U35234	Protein tyrosine phosphatase sigma	M
U43843	H-neuro-d4 protein	M
U64871	Putative G protein-coupled receptor (GPR19)	L
U66198	Fibroblast growth factor homologous factor 2 (FHF-2)	M
U79247	Clone 23599	LM
U81262	Lerk-5 (Lerk-5)	LM
X95425	EHK-1 receptor tyrosine kinase	L
Z11933	N-Oct 3, N-Oct5a, and N-Oct 5b proteins	M
Z70220	Unknown protein (clone ICRFp507O0882)	M

Uniquely Expressed in Adult Pancreas

AF014958	Chemokine receptor X (CKRX)	LM
D31797	CD40 ligand (CD40L)	LM
J00268	Insulin	H
J02883	Colipase	H
J05125	Triglyceride lipase	H
L08010	Reg gene homologue	H
L14813	Carboxyl ester lipase like protein (CELL)	MH
M16652	Pancreatic elastase IIA	H
M16653	Elastase IIB	H
M21056	Pancreatic phospholipase A-2 (PLA-2)	H
M22612	Pancreatic trypsin 1 (TRY1)	H
M24349	Parathyroid hormone-like protein (PLP)	L
M24400	Chymotrypsinogen	H
M55131	Cystic fibrosis transmembrane conductance regulator (CFTR)	M
M74096	Long chain acyl-CoA dehydrogenase (ACADL)	L
M81057	Procarboxypeptidase B	H
M93284	Pancreatic lipase related protein 2 (PLRP2)	H
S82198	Caldecrin, serum calcium-decreasing factor	H
X54457	Bile-salt-stimulated lipase (BSSL)	H
X67318	Procarboxypeptidase A1	H
X71877	Chymotrypsin-like protease CTRL-1	H
Y00705	Pancreatic secretory inhibitor (expressed in neoplastic tissue)	H
Y08134	ASM-like phosphodiesterase 3b	LM

* The abundance levels in copies per cell: L <5, LM >5<10, M >10 <50, MH >50 <100, H >100.

Conclusion

The present invention provides methods and compositions for identifying and using maintenance genes. It is to be understood that the above description is intended to be illustrative and not restrictive. Many variations of the invention will be apparent to those of skill in the art upon reviewing the above description. By way of example, the invention has been described primarily with reference to the use of a high density oligonucleotide array, but it will be readily recognized by those of skill in the art that other nucleic acid arrays, other methods of measuring transcript levels and gene expression monitoring at the protein level could be used. The scope of the invention should, therefore, be determined not with reference to the above description, but should instead be determined with reference to the appended claims, along with the full scope of equivalents to which such claims are entitled.

All references cited in this application are incorporated by reference for all purposes.

What is claimed is:

1. A method for identifying a maintenance gene comprising:
determining the expression of at least one hundred genes in at least two different
5 types of tissues in two different developmental stages; and
indicating a gene that is expressed at the same level in said tissues in said stages
as said maintenance gene.
2. The method of Claim 1 wherein said at least one hundred genes comprise at least
one thousand genes.
- 10 3. The method of Claim 1 wherein said at least two types of tissues comprise at least
five different types of tissues.
4. The method of Claim 1 wherein said determining uses nucleic acid probe arrays.
5. The method of Claim 1 wherein a gene is considered as expressed at the same
level if the variation of its expression is within 10 fold.
- 15 6. The method of Claim 5 wherein a gene is considered as expressed at the same
level if the variation of its expression is within 5 fold.
7. The method of Claim 6 wherein a gene is considered as expressed at the same
level if the variation of its expression is within 2 fold.
8. The method of Claim 1 wherein a gene is considered as expressed at the same
20 level if the variation of its expression is not statistically significant.
9. A method for comparing the expression of a gene in a plurality of biological
samples comprising:

measuring the expression of at least three maintenance genes selected from the group consisted of:

HG2815- HT2931	Myosin, Light Chain, Alkali,(Gb:U02629), Alt. Splice 2
J03191	Profilin
M10277	Cytoplasmic beta-actin
M14483	PTMA gene extracted from prothymosin alpha
M17733	Thymosin beta-4 mRNA
M19283	Cytoskeletal gamma-actin
M26708	Prothymosin alpha mRNA (ProT-alpha)
S65738	Actin depolymerizing factor
U37122	Adducin gamma subunit
X00351	Beta-actin
X54304	Myosin regulatory light chain
X95404	Non-muscle type cofilin
D15057	DAD-1
L08246	Myeloid cell differentiation protein (MCL1)
M63379	TRPM-2 protein, Clusterin
D13118	ATP synthase subunit c encoded by P1
D14710	ATP synthase alpha subunit
D16469	Vacuolar ATP synthase subunit AC45 precursor
D16562	ATP synthase gamma-subunit (L-type)
D49400	Fetus brain vacuolar ATPase
M19483	ATP synthase beta subunit
M37104	Mitochondrial ATPase coupling factor 6 subunit (ATP5A)
U09813	Mitochondrial ATP synthase subunit 9, P3 gene copy
U16799	NaK-ATPase beta-1 subunit
U51478	Sodium/potassium-transporting ATPase beta-3 subunit
X60221	H+-ATP synthase subunit b
X64330	ATP-citrate lyase
X83218	ATP synthase
Z71460	Vacuolar-type H(+)-ATPase 115 kDa subunit
AB001325	AQP3 aquaporine 3 (water channel)
L06132	Voltage-dependent anion channel isoform 1 (VDAC)
L08666	Porin (por)
AC002115	COX6B (COXG)
J04823	Cytochrome c oxidase subunit VIII (COX8)
J04973	Cytochrome bc-1 complex core protein II
L32977	Clone f17252 ubiquinol cytochrome c reductase Rieske iron-

sulphur protein (UQCRFS1)
 U90915 Clone 23600 cytochrome c oxidase subunit IV
 X13238 Cytochrome c oxidase subunit VIc
 X15341 COX VIa-L cytochrome c oxidase liver-specific subunit VIa (EC 1.9.3.1)
 X15822 COX VIIa-L liver-specific cytochrome c oxidase (EC 1.9.3.1.)
 X16560 COX VIIc subunit VIIc of cytochrome c oxidase (EC 1.9.3.1)
 Z14244 CoxVIIIb cytochrome c oxidase subunit VIIIb
 D50310 Cyclin I
 D89667 C-myc binding protein
 M93651 SET (Suvar3-9, Enhancer-of-zeste, Trithorax)
 X61123 BTG1 mRNA, B-cell translocation gene 1
 D43682 Very-long-chain acyl-CoA dehydrogenase (VLCAD)
 D55654 Cytosolic malate dehydrogenase
 D90086 Pyruvate dehydrogenase (EC 1.2.4.1) beta subunit
 M91432 Medium-chain acyl-CoA dehydrogenase (MCAD)
 X01677 Liver glyceraldehyde-3-phosphate dehydrogenase (G3PD EC 1.2.1.12)
 X02152 Lactate dehydrogenase-A (LDH-A EC 1.1.1.27)
 X05409 RNA mitochondrial aldehyde dehydrogenase I ALDH I (EC 1.2.1.3)
 X13794 Lactate dehydrogenase B exon 1 and 2 (EC 1.1.1.27)
 D78134 Glycine-rich RNA binding protein CIRP
 D90209 DNA binding protein TAXREB67
 HG4264- HT4534 Guanine Nucleotide-Binding Protein Rab5c-Like Protein
 HG662-HT662 Epstein-Barr Virus Small Rna-Associated Protein
 J03827 Y box binding protein-1 (YB-1)
 L37368 (Clone E5.1) RNA-binding protein
 L43631 Scaffold attachment factor (SAF-B)
 M21142 Guanine nucleotide-binding protein G-s-alpha-3 extracted from guanine nucleotide-binding protein alpha-subunit (G-s-alpha)
 M23613 Nucleophosmin
 M34539 FK506-binding protein (FKBP)
 S78771 NAT=CpG island-associated [1741 nt]
 U02493 54 kDa protein, 54 KD Nuclear RNA binding protein
 U07857 18 kDa Alu RNA binding protein
 U10439 Double-stranded RNA adenosine deaminase
 U20998 Signal recognition particle subunit 9 (SRP9)

U30827 Splicing factor SRp40-3 (SRp40)
 U33818 Inducible poly(A)-binding protein
 U33821 Tax1-binding protein TXBP151
 U38846 Stimulator of TAR RNA binding (SRB)
 U51334 Putative RNA binding protein (RBP56)
 U68105 Poly(A)-binding protein (PABP)
 U79528 SR31747 binding protein 1
 X04347 DNA binding protein UPI homologue (C-terminus)
 X63753 Son-a
 X71428 Fus, RNA binding protein
 X75252 Phosphatidylethanolamine binding protein
 Z48501 Polyadenylate binding protein II
 Z71460 Vacuolar-type H(+)-ATPase 115 kDa subunit.
 D78132 Ras homologue enriched in brain (RHEB) Ras-related GTP binding protein
 HG4264- Guanine Nucleotide-Binding Protein Rab5c-Like Protein
 HT4534
 L25080 GTP-binding protein (rhoA)
 L33075 Ras GTPase-activating-like protein (IQGAP1)
 M21142 Guanine nucleotide-binding protein G-s-alpha-3
 M24194 MHC protein homologous to chicken B complex protein
 U20285 Gps1 (GPS1), G PROTEIN PATHWAY SUPPRESSOR 1
 U41654 Adenovirus protein E3-14.7k interacting protein 1 (FIP-1)
 D32129 HLA class-I (HLA-A26) heavy chain (clone cMIY-1)
 D49824 HLA-B null allele
 M59830 MHC class III HSP70-2 (HLA)
 X75091 HLA-DR associated protein II (PHAPII)
 HG2855- Heat Shock Protein 70 Kda (Gb:Y00371)
 HT2995
 J04988 90 kD heat shock protein
 M11717 Heat shock protein (hsp 70)
 X15183 90-kDa heat-shock protein
 Z23090 28 kDa heat shock protein
 L20941 Ferritin heavy chain, iron storage
 M11147 Ferritin L chain, iron storage
 M69023 Globin
 L19779 Histone H2A.2
 M11353 Histone class C
 M37583 Histone (H2A.Z)
 U50079 Histone deacetylase HD1
 X05855 Histone H3.3 exon 2

X13546	HMG-17 protein
X72841	IEF 7442, Histone acetyl transferase type B subunit 2
Z48950	HH3.3B histone H3.3
X57351	1-8D from interferon-inducible family
X59892	IFN-inducible gamma2 protein
K03515	Neuroleukin
L76191	Interleukin-1 receptor-associated kinase (IRAK)
HG1153-	Nucleoside Diphosphate Kinase Nm23-H2s
HT1153	
L36151	Phosphatidylinositol 4-kinase
L40027	Glycogen synthase kinase 3
L76191	Interleukin-1 receptor-associated kinase (IRAK)
M14676	Src-like kinase (slk)
M30448	Casein kinase II beta subunit
M33336	CAMP-dependent protein kinase type I-alpha subunit (PRKAR1A)
U40282	Integrin-linked kinase (ILK)
U51004	Putative protein kinase C inhibitor (PKCI-1)
U77948	Bruton tyrosine kinase-associated protein-135
V00572	Encoding phosphoglycerate kinase
X56468	14.3.3 protein a protein kinase regulator
X57152	Casein kinase II subunit beta (EC 2.7.1.37)
D10522	80K-L protein
HG1862-	Calmodulin Type I
HT1897	
M19311	Calmodulin
X57346	HS1 protein
AJ000099	Lysosomal hyaluronidase
J04182	Lysosomal membrane glycoprotein-1 (LAMP1)
M15182	Beta-glucuronidase
M29877	Alpha-L-fucosidase
U91932	AP-3 complex sigma3A subunit
HG658-HT658	Major Histocompatibility Complex Class I C (Gb:X58536)
J00105	Beta-2 microglobulin
M11313	Alpha-2-macroglobulin
S82297	Beta 2-microglobulin
M84349	Transmembrane protein (CD59)
X59405	Membrane cofactor protein
D13315	Lactoyl glutathione lyase
D49489	Protein disulfide isomerase-related protein P5
D78361	Ornithine decarboxylase antizyme ORF 1 and ORF 2

D85758	Protein homologous to DROER protein, Enhancer of rudimentary homolog
HG2279- HT2375	Triosephosphate Isomerase
HG4073- HT4343	Cytosolic Acetoacetyl-Coenzyme A Thiolase
J03077	Co-beta glucosidase (proactivator)
J03459	Leukotriene A-4 hydrolase
J04173	Phosphoglycerate mutase (PGAM-B)
L19437	Transaldolase containing transposable element
L48513	Paraoxonase 2 (PON2)
M14328	Alpha enolase
M32405	Homologue of rat insulinoma gene (rig), exons 4
M33764	Ornithine decarboxylase
M37721	Peptidylglycine alpha-amidating monooxygenase
M83088	Phosphoglucomutase 1 (PGM1)
M86400	Phospholipase A2
U29607	Methionine aminopeptidase
U31930	Deoxyuridine nucleotidohydrolase
U44772	Palmitoyl protein thioesterase
U67171	Selenoprotein W (selW)
U86070	Phosphomannomutase
U94586	NADH:ubiquinone oxidoreductase MLRQ subunit
U97105	Drp2, Dihydropyrimidinase related protein
X02317	Cu/Zn superoxide dismutase (SOD)
X05130	Prolyl 4-hydroxylase beta subunit (EC 1.14.11.2) (procollagen-L-proline, 2-oxoglutarate:oxygen oxidoreductase, 4-hydroxylating)
X12447	Aldolase A gene (EC 4.1.2.13)
X14448	GLA alpha-D-galactosidase A
X52851	Peptidylprolyl isomerase gene extracted from cyclophilin gene (EC 5.2.1.8)
X71973	GPx-4 phospholipid hydroperoxide glutathione peroxidase
Y09616	Putative carboxylesterase
Z15115	TOP2, DNA topoisomerase II
Z49835	Protein disulfide isomerase
L11066	Mitochondrial stress-70 protein precursor
M22382	Mitochondrial matrix protein P1 (nuclear encoded)
M22538	Nuclear-encoded mitochondrial NADH-ubiquinone reductase 24Kd subunit
M22760	Nuclear-encoded mitochondrial cytochrome c oxidase Va subunit

M26730 Mitochondrial ubiquinone-binding protein 5' flank with an LTR-like sequence
M37104 Mitochondrial ATPase coupling factor 6 subunit (ATP5A)
M94556 Mitochondrial specific single stranded DNA binding protein
U54778 14-3-3 epsilon, Mitochondrial import stimulation factor L
U62739 Branched-chain amino acid aminotransferase (ECA40), Mitochondrial precursor
X05409 Mitochondrial aldehyde dehydrogenase I ALDH I (EC 1.2.1.3)
X60036 Mitochondrial phosphate carrier protein
Y00764 Mitochondrial hinge protein
Z70759 Mitochondrial 16S rRNA
M14200 Diazepam binding inhibitor (DBI)
J03805 Phosphatase 2A
X68277 CL 100 protein tyrosine phosphatase
X74008 Protein phosphatase 1 gamma
X81003 HCG V
U37690 RNA polymerase II subunit (hsRBP10)
Z27113 RNA polymerase II subunit 14.4 kD
Z47727 RNA polymerase II subunit
HG417-HT417 Cathepsin B
L02426 26S protease (S4) regulatory subunit
M23254 Ca2-activated neutral protease large subunit (CANP)
M27891 Cystatin C (CST3)
U14394 Tissue inhibitor of metalloproteinases-3, TIMP3
U46692 Cystatin B gene
X12451 MrRNA pro-cathepsin L (major excreted protein MEP)
D00761 Proteasome subunit HC5
D00762 Proteasome subunit HC8
D00763 Proteasome subunit HC9
D26598 Proteasome subunit HsC10-II
D26599 Proteasome subunit HsC7-I
D26600 Proteasome subunit HsN3
D29012 Proteasome subunit Y
D38047 26S proteasome subunit p31
D38048 Proteasome subunit z
D50063 Proteasome subunit p40_ / Mov34 protein
M64992 Prosomal protein P30-33K (pros-30)
U70735 34 kDa mov34 isologue
X61970 Macropain subunit zeta, Proteasome Zeta chain
X95586 MB1

D23673	Clone HH109 (screened by the monoclonal antibody of insulin receptor substrate-1 (IRS-1))
L40357	Thyroid receptor interactor (TRIP7)
M14199	Laminin receptor (2H5 epitope)
M88279	Immunophilin (FKBP52), P59 Protein (HSP binding immunophilin) (HBI)
M88458	ELP-1, Er lumen protein retaining receptor 2 (KDEL receptor 2)
U43901	37 kD laminin receptor precursor/p40 ribosome associated protein
U72511	B-cell receptor associated protein (hBAP)
X07979	Fibronectin receptor beta subunit
X80763	5-HT _{2c} receptor
Z32765	CD36
M16447	Dihydropteridine reductase (hDHPR) mRNA
M28713	NADH-cytochrome b5 reductase (b5R)
X15414	Aldose reductase
X91247	Thioredoxin reductase
U49785	D-dopachrome tautomerase
J05249	Replication protein A 32-kDa subunit
X15729	Nuclear p68 protein
L20688	RHO GDP-dissociation inhibitor protein (Ly-GDI)
U02570	CDC42 GTPase-activating protein
Z24725	Mitogen inducible mig-2
HG1322- HT5143	Small Nuclear Ribonucleoprotein Polypeptide C Alt. Splice 2
HG3076- HT3238	Heterogeneous Nuclear Ribonucleoprotein K Alt. Splice 1
J04615	Lupus autoantigen (small nuclear ribonucleoprotein snRNP SM-D)
L03532	M4 protein, Heterogeneous Nuclear Ribonucleoprotein M
L22009	HnRNP H mRNA
L28010	HnRNP F protein mRNA
M16342	Nuclear ribonucleoprotein particle (hnRNP) C protein
M21259	Alu repeats in the region 5' to the small nuclear ribonucleoprotein E
M29064	HnRNP B1 protein
M74002	Arginine-rich nuclear protein
M88108	P62
M94630	HnRNP-C like protein
U00947	Heterogeneous Nuclear Ribonucleoprotein A1
U15008	SnRNP core protein Sm D2

X12671	Heterogeneous nuclear ribonucleoprotein (hnRNP) core protein A1
X16135	Novel heterogeneous nuclear RNP protein L protein
X78136	HnRNP-E2
D14530	Homolog of yeast ribosomal protein S28
D23660	Ribosomal protein
D79205	Ribosomal protein L39
D87735	Ribosomal protein L14
HG1800- HT1823	Ribosomal Protein S20
HG2873- HT3017	Ribosomal Protein L30 Homolog
HG311-HT311	Ribosomal Protein L30
HG3364- HT3541	Ribosomal Protein L37
HG33-HT33	Ribosomal Protein S4, X-Linked
HG384-HT384	Ribosomal Protein L26
HG4319- HT4589	Ribosomal Protein L5
HG4542- HT4947	Ribosomal Protein L10
HG613-HT613	Ribosomal Protein S12
HG821-HT821	Ribosomal Protein S13
L04483	Ribosomal protein S21 (RPS21)
L06499	Ribosomal protein L37a (RPL37A)
L06505	Ribosomal protein L12
L11566	Ribosomal protein L18 (RPL18)
L19527	Ribosomal protein L27 (RPL27)
L38941	Ribosomal protein L34 (RPL34)
M13934	Ribosomal protein S14
M15661	Ribosomal protein
M17885	Acidic ribosomal phosphoprotein P0
M17886	Acidic ribosomal phosphoprotein P1
M18000	Ribosomal protein S17
M31520	Ribosomal protein S24
M36072	Ribosomal protein L7a (surf 3) large subunit
M60854	Ribosomal protein S16
M64716	Ribosomal protein S25
M77232	Ribosomal protein S6
M81757	S19 ribosomal protein
U09953	Ribosomal protein L9
U12404	Csa-19

U12465	Ribosomal protein L35
U14968	Ribosomal protein L27a
U14969	Ribosomal protein L28
U14970	Ribosomal protein S5
U14971	Ribosomal protein S9
U14972	Ribosomal protein S10
U14973	Ribosomal protein S29
U25789	Ribosomal protein L21
U58682	Ribosomal protein S28
U78027	L44L (L44-like ribosomal protein)
X03342	Ribosomal protein L32
X06617	Ribosomal protein S11
X15940	Ribosomal protein L31
X17206	LLRep3, 40S RIBOSOMAL PROTEIN S2
X52966	Ribosomal protein L35a
X53777	L23 putative ribosomal protein
X55715	Hums3 40S Ribosomal protein s3
X55954	HL23 ribosomal protein homologue
X56932	23 kD highly basic protein
X57959	Ribosomal protein L7
X62691	Ribosomal protein (homologous to yeast S24)
X63527	Ribosomal protein L19
X64707	BBC1
X67247	RpS8 gene for ribosomal protein S8
X69150	Ribosomal protein S18
X69391	Ribosomal protein L6
X69654	Ribosomal protein S26
X73460	Ribosomal protein L3
X79234	Ribosomal protein L11
Z12962	Homologue to yeast Ribosomal protein L41
Z25749	Gene for ribosomal protein S7
Z26876	Ribosomal protein L38
Z28407	Ribosomal protein L8
Z49148	Ribosomal protein L29
M36341	ADP-ribosylation factor 4 (ARF4)
M74491	ADP-ribosylation factor 3
M84332	ADP-ribosylation factor 1
U70439	Silver-stainable protein SSP29
X04526	Liver beta-subunit signal transducing proteins Gs/Gi (beta-G)
D28915	Hepatitis C-associated microtubular aggregate protein p44

D38549	KIAA0068
HG1980- HT2023	Tubulin, Beta 2
HG2238- HT2321	Nuclear Mitotic Apparatus Protein 1 Alt. Splice 2
HG3514- HT3708	Tropomyosin Tm30nm, Cytoskeletal
HG987-HT987	Mac25
L11373	Protocadherin 43, PC43
L14837	Tight junction (zonula occludens) protein ZO-1
M20471	Brain-type clathrin light-chain a mRNA
M31013	Nonmuscle myosin heavy chain (NMHC)
M33308	Vinculin mRNA
M33680	26-kDa cell surface protein TAPA-1, CD81 ANTIGEN
M55998	Alpha-1 collagen type I gene, 3' end
M57710	LgE-binding protein (epsilon-BP)
M69066	Moesin
M69181	Nonmuscle myosin heavy chain-B (MYH10)
M96803	Ral beta-spectrin (SPTBN1)
S54005	Thymosin beta-10 [, metastatic melanoma cell line, 453 nt]
U03100	Alpha2(E)-catenin
U24105	Coatamer protein (HEPCOP)
U45976	Clathrin assembly protein lymphoid myeloid leukemia (CALM)
U56637	Capping protein alpha subunit isoform 1, F-actin capping protein alpha-1 subunit (CAPZ)
U57341	Neurofilament triplet L protein
U60115	Skeletal muscle LIM-protein SLIM1
U83463	Scaffold protein Pbp1
V00599	Beta-tubulin (from clone D-beta-1)
X51521	Ezrin
X53331	Matrix Gla protein
X57398	PM5 protein
X72964	Caltractin
X82103	Beta-COP, coatamer protein
X97074	MRNS for clathrin-associated protein
Z19554	Vimentin
Z24727	Tropomyosin isoform
Z47038	Putative microtubule-associated; protein 1A (MAP1A)
J03473	Poly(ADP-ribose) synthetase
U09510	Glycyl-tRNA synthetase
U43286	Selenophosphate synthetase 2 (SPS2)

U79262	Deoxyhypusine synthase
X76013	QRSHs glutaminyl-tRNA synthetase
X91257	Seryl-tRNA synthetase
X94754	Yeast methionyl-tRNA synthetase homologue
Z47055	CDNA sequence farnesyl pyrophosphate synthetase like-4
HG1515- HT1515	Transcription Factor Btf3b
HG4297- HT4567	Transcriptional Coactivator Pc4
L12168	Adenylyl cyclase-associated protein (CAP)
L20298	Transcription factor (CBFB)
L34587	RNA polymerase II elongation factor SIII, p15 subunit
L49380	Transcription factor ZFM1
M81601	Transcription elongation factor (SII)
M97935	Transcription factor ISGF-3
U10323	Nuclear factor NF45
U14193	TFIIA gamma subunit mRNA
U95040	Transcriptional corepressor hKAP1/TIF1B
X52882	T-complex polypeptide 1
X80909	Alpha NAC
Z47087	RNA polymerase II elongation factor-like protein
D26535	Dihydrolipoamide succinyltransferase (exon 1-15)
L10413	Farnesyltransferase alpha-subunit mRNA
M24485	Glutathione S-transferase pi (GSTP1)
U56417	Lysophosphatidic acid acyltransferase-alpha
U90313	Glutathione-S-transferase homolog
D13413	Tumor-associated 120 kDa nuclear protein p120 (carboxyl terminus)
D61380	DJ-1 protein
HG1102- HT1102	Ras-Related C3 Botulinum Toxin Substrate
HG3549- HT3751	Wilm'S Tumor-Related Protein
HG4541- HT4946	Transformation-Related Protein
M15990	C-yes-1, Proto-oncogene tyrosine protein kinase YES
M55409	Pancreatic tumor-related protein
M84711	V-fos transformation effector protein (Fte-1)
S79219	Metastasis-associated
U50523	BRCA2 region sequence CG037
U57342	Myelodysplasia/myeloid leukemia factor 2 (MLF2)
V01512	Cellular onco c-fos (sequence)

X16064	Translationally controlled tumor protein
X16416	C-abl encoding p150 protein, Proto-oncogene tyrosine protein kinase ABL
X56681	JunD
X67951	Proliferation-associated gene (pag)
X72727	Tunp transformation upregulated nuclear protein
X81817	BAP31, CDM Protein (6C6-AG Tumor associated antigen)
D30655	Eukaryotic initiation factor 4AII
J04617	Elongation factor EF-1-alpha
L26247	Sui1s01
U46025	Translation initiation factor eIF-3 p110 subunit
U62962	Int-6, Viral integration site protein INT-6
U94855	Translation initiation factor 3 47 kDa subunit
X03689	Fragment elongation factor TU (N-terminus)
X51466	Elongation factor 2
X55733	Initiation factor 4B
X60489	Elongation factor-1-beta
Z21507	EF-1delta gene encoding elongation factor-1-delta
Z37166	BAT1, nuclear RNA helicase (DEAD family)
AB002533	Qip1
AJ001421	Rer1 protein
J02683	ADP/ATP carrier protein
J03592	ADP/ATP translocase, clone pHAT8
M28209	TGTP-binding protein (RAB1)
M34175	Beta adaptin mRNA
U32944	Cytoplasmic dynein light chain 1 (hdlc1)
U36341	SLC6A8 (creatine transporter)
U41740	Trans-Golgi p230
U51478	Sodium/potassium-transporting ATPase beta-3 subunit
U61734	Protein trafficking protein (S31iii125)
U70660	Copper transport protein HAH1 (HAH1)
X74104	TRAP beta subunit, Translocon-associated protein
Y00281	Ribophorin I
Y00282	Ribophorin II
Z69043	Translocon-associated protein delta subunit precursor
D23662	Ubiquitin-like protein
L10284	Integral membrane protein calnexin (IP90)
M26880	Ubiquitin
M58028	Ubiquitin-activating enzyme E1 (UBE1)
S79522	Ubiquitin carboxyl extension protein [540 nt]
U39317	E2 ubiquitin conjugating enzyme UbcH5B (UBCH5B)

U44839	Putative ubiquitin C-terminal hydrolase (UHX1)
U46751	Phosphotyrosine independent ligand p62 the Lck SH2 domain
U49869	Ubiquitin
X56997	UbA52 coding ubiquitin-52 amino acid fusion protein
HG3214-	Metallopanstimulin 1
HT3391	
L11672	Kruppel related zinc finger protein (HTF10)
M94046	Zinc finger protein (MAZ)
X70394	OZF
AC002045	A-589H1.2 from Chromosome 16 BAC clone CIT987-SKA-589H1
D13641	KIAA0016
D14658	KIAA0102
D14662	KIAA0106
D14694	KIAA0024
D14695	KIAA0025
D14812	KIAA0026
D21260	KIAA0034
D21261	KIAA0120
D21853	KIAA0111
D25274	Unknown function
D26068	KIAA0038
D29643	KIAA0115
D31767	KIAA0058
D31883	KIAA0059
D31890	KIAA0070
D42043	KIAA0084
D43950	KIAA0098
D63476	KIAA0142
D63477	KIAA0143
D63478	KIAA0144
D63878	KIAA0158
D63878	KIAA0158
D79986	KIAA0164
D79994	KIAA0172
D80005	KIAA0183
D84294	TPRDI, maps to Down's syndrome region
D86963	KIAA0208
D86974	KIAA0220
D87451	KIAA0262

D87953	RTP, Tunicamycin responsive protein
L20773	In the region near the btk involved in a-gamma-globulinemia
L40391	Clone s153
L40395	Clone S20iii15
L40397	Clone S31i125
S73591	VDUP1, vitamin D(3) up-regulated protein 1
S77356	Transcript ch21=oligomycin sensitivity conferral protein oscp homolog
U34343	13kD differentiation-associated protein
U72342	Platelet activating factor acetylhydrolase brain isoform 45 kDa subunit (LIS1)
U79254	Clone 23693
U79294	Clone 23748
U81556	Hypothetical protein A4
U90909	Clone 23722 sequence
X14684	La protein C-terminal region
X15187	Tra1 homologue of murine tumor rejection antigen gp96
X62654	Me491/CD63 antigen gene
X75861	TEGT, testis-enhanced gene transcript
X80822	ORF
X83416	PrP exon 2
Z11793	Selenoprotein P
D86479	AEBP1
AB001106	Glia maturation factor
D13370	APX encoding APEX nuclease
D14043	MGC-24, mucin-like glycoprotein
D63506	Unc-18homologue, Syntaxin binding protein
D63851	Unc-18 homologue
D78129	Adult (34 year old) Male liver squalene epoxidase
HG1869-	Male Enhanced Antigen
HT1904	
HG2917-	Major Histocompatibility Complex Class I E (Gb:M21533)
HT3061	
HG3342-	Ld1
HT3519	
HG3597-	Major Histocompatibility Complex Class I (Gb:X12432)
HT3800	
HG3638-	Amyloid Beta (A4) Precursor Protein, Alt. Splice 2, A4(751)
HT3849	
HG651-HT4201	Adducin, Alpha Subunit, Alt. Splice 2
J04456	14 kd lectin
L09209	Amyloid protein homologue

M13450	Esterase D
M60858	Nucleolin
M63483	Major nuclear matrix protein
M86667	NAP (nucleosome assembly protein)
U01691	Annexin V (ANX5) gene, 5'-untranslated region
U06155	Chromosome 1q subtelomeric sequence D1S553
U11861	G10 homolog (edg-2)
U35048	TSC-22 protein
U41635	OS-9 precursor
U46570	Tetratricopeptide repeat protein (tpr1)
U50733	Dynamitin mRNA
U62317	Hypothetical protein 384D8_2 extracted from Chromosome 22q13
U73824	P97
V00594	Metallothionein from cadmium-treated cells
X66397	Tpr
X73358	HAES-1, GRG protein (ESP1 protein) -Amino enhancer of split
X76534	NMB
X77584	ATL(Adult T cell leukemia)-derived factor/thioredoxin
X80199	MLN51
X80200	MLN62
X82456	MLN50
X87838	Beta-catenin
X96484	DGCR6 protein
X98482	TNNT2 (troponin)
Y00264	Amyloid A4 precursor of Alzheimer disease
Y00433	Glutathione peroxidase
Z35093	SURF-1
Z93784	Mouse Brain Protein E46 like sequences ESTs

and

evaluating said expression of said gene in said plurality of samples using the expression of said at least three maintenance genes.

- 5 10. The method of Claim 9 wherein said at least three maintenance genes comprise at least five maintenance genes selected from said group.

11. The method of Claim 10 wherein said at least five maintenance genes comprise at least ten maintenance genes selected from said group.
12. The method of Claim 9 wherein said evaluating comprises calculating expression ratio of said gene over said maintenance genes.

ABSTRACT

This invention provides methods for discovering maintenance genes and for using maintenance genes. In one embodiment, the expression of at least three maintenance genes are measured and used as reference (or control) for comparing the expression of target genes in two or more biological samples.